REMARKS

Claims 1-32 are pending. For the Examiner's convenience, responses herein have been numbered to correspond to the appropriate rejection in the Office Action. It should be noted that the correct Attorney Docket No. for this application is "77670/593."

Specification/Informalities

[14] Applicants traverse the assertion that the disclosure of sequence $D_1D_2X_1(X_2X_3)X_4D_3$ is new matter. Applicants submit that the disclosure in the original patent of sequence $D_1D_2X_1X_2(X_3X_4)D_3$ encompasses sequence $D_1D_2X_1(X_2X_3)X_4D_3$. Hence, Applicants submit that the sequence algorithm $D_1D_2X_1(X_2X_3)X_4D_3$ is fully supported in the specification.

First, Applicants submit that a review of the algorithm $D_1D_2X_1X_2(X_3X_4)D_3$, as provided in the specification, reveals to one of skill in the art that the expressly disclosed algorithm additionally encompasses the sequence $D_1D_2X_1(X_2X_3)X_4D_3$. Applicants disclose the algorithmic domain sequence $D_1D_2X_1(X_2X_3)X_4D_3$ as a sequence of the aspartic-acid rich domain of any prenyl diphosphate synthase by expressly teaching the algorithm $D_1D_2X_1X_2(X_3X_4)D_3$, where X denotes any amino acid and where X_3 and X_4 may or may not be present. *See* column 4, line 11. Applicants submit this algorithm encompasses $D_1D_2X_1(X_2X_3)X_4D_3$.

In the sequence $D_1D_2X_1X_2(X_3X_4)D_3$, if X_3 and X_4 are not present, the resulting sequence is $D_1D_2X_1X_2D_3$. If X_2 is then defined as X_4 (since X may be defined as any amino acid) the resulting sequence is $D_1D_2X_1X_4D_3$. Because the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ becomes $D_1D_2X_1X_4D_3$ when X_2 and X_3 are not present, one of skill in the art would recognize that the sequence algorithm expressly disclosed by Applicants, $D_1D_2X_1X_2(X_3X_4)D_3$, also encompasses the sequence $D_1D_2X_1(X_2X_3)X_4D_3$. Further, since each of X_1 to X_4 is defined as any amino acid, one of skill in the art would recognize that the aspartic acid-rich domain $D_1D_2X_1X_2(X_3X_4)D_3$ provided in the specification at column 4, line 11 may be represented as any of $D_1D_2X_1X_2(X_3X_4)D_3$ or $D_1D_2X_1(X_2X_3)X_4D_3$ or $D_1D_2(X_1X_2)X_3X_4D_3$ depending on how each of X_1 to X_4 is defined. Therefore, the sequence $D_1D_2X_1X_2(X_3X_4)D_3$ as disclosed in the specification expressly includes the sequence $D_1D_2X_1(X_2X_3)X_4D_3$.

Next, Applicants also expressly disclose examples of prenyl diphosphate synthases of the invention having an aspartic-acid rich domain of $D_1D_2X_1(X_2X_3)X_4D_3$ and synthesizing farnesyl

diphosphate with a shorter chain length than those synthesized by wild-type prenyl diphosphate synthases.

For example, Applicants provide the aspartic acid-rich domain I of geranylgeranyl diphosphate synthase of *Sulfolobus acidocaldarius*, which has the sequence DDIMD. *See* Figure 1 and column 4, lines 60-67. The sequence DDIMD corresponds to the algorithm $D_1D_2X_1X_4D_3$.

Applicants then provide five mutants of the geranylgeranyl diphosphate synthase *Sulfolobus acidocaldarius*. *See* column 6, lines 48-63. While each of mutants 1-4 have the same aspartic acid-rich domain I sequence as the wild-type, DDIMD ($D_1D_2X_1X_4D_3$), mutant five has the aspartic acid-rich domain I sequence of DDLPSMD ($D_1D_2X_1(X_2X_3)X_4D_3$), where X_1 is substituted with L and X_2 and X_3 are present as P and S. Applicants further provide evidence that mutant 5 synthesizes farnesyl diphosphate with a shorter chain length than those synthesized by wild-type geranylgeranyl diphosphate synthase of *Sulfolobus acidocaldarius*. *See* Figure 1.

Applicants also disclose the wild-type aspartic acid-rich domain I sequence of geranylgeranyl diphosphate synthase of *Arabidopsis thaliana* having the sequence DDLPCMD ($D_1D_2X_1(X_2X_3)X_4D_3$). *See* Figure 1 and column 4, lines 60-67. The sequence of *Arabidopsis thaliana* is nearly identical to that of mutant 5 of *Sulfolobus acidocaldarius*, DDLPSMD. The only difference exists at the X_3 position where C corresponds to S. One of skill in the art would recognize that C and S would behave very similarly in this particular domain since the only difference between these two amino acids is the substitution of a sulfur for an oxygen in the hydroxyl group. As a result, one of skill in the art would expect these domains to synthesize farnesyl diphosphates with chains lengths of similar size relative to mutants within the same prenyl diphosphate synthase.

The domains of *Arabidopsis thaliana* and mutant 5 of *Sulfolobus acidocaldarius* are further analogous in that the 5 amino acid residues to the N-terminal side of the domains of interest are identical but for a difference of an M and a T in the fifth position to the N-terminal side of the domain. *See* Figure 1. As a result, one of skill in the art would be bolstered in the view that the two enzymes would synthesize similarly sized farnesyl diphosphate.

In Figure 3, data is provided for the chain length of farnesyl diphosphate synthesized by mutant 5 of *Sulfolobus acidocaldarius*. No data is likewise provided for *Arabidopsis thaliana*. However, since these domains are nearly identical (and these domains have been identified as determining length of synthesized farnesyl diphosphate chains) one of skill in the art would

expect the domains to similarly effect the length of farnesyl diphosphate chains synthesized from these enzymes.

In Figure 3, mutant 5 of *Sulfolobus acidocaldarius* is shown to produce some longer chains and some shorter chains of farnesyl diphosphate, while mutants 1-4 produce only shorter chains. One of skill in the art, would expect, then, that *Arabidopsis thaliana* would produce some long chains and some short chains or perhaps chains of intermediate length as compared to the wild-type of *Sulfolobus acidocaldarius*.

One of skill in the art would then consider what farnesyl disphosphate chain length would be synthesized by the geranylgeranyl diphosphate synthase of *Arabidopsis thaliana* if it underwent substitution at the X_2 and X_3 positions resulting in the sequence $D_1D_2X_1(X_2X_3)X_4D_3$, where X_2 and X_3 have been removed. One of skill would understand that the resulting domain sequence would be analogous to the sequences of mutants 1-4 of *Sulfolobus acidocaldarius*. *See* column 6, lines 48-59. Each of these sequences synthesized farnesyl diphosphate chains that were shorter than mutant 5. *See* Figure 3. As a result, one of skill in the art would likewise expect the farnesyl diphosphate chains synthesized by a mutant of *Arabidopsis thaliana*, where the X_2 and X_3 positions had been removed, to be shorter than the wild-type.

Upon review of all of this data, then, one of skill in the art would recognize that Applicants disclosed the sequence of $D_1D_2X_1(X_2X_3)X_4D_3$ in *Arabidopsis thaliana* and demonstrated by analogy that if X_2 and X_3 were to be removed, synthesis of farnesyl diphosphate would result in shorter chains than the wild-type where X_2 and X_3 had not been removed.

Further, one of skill in the art would recognize that the foregoing analysis not only applies to the first sequence in Figure 1 (*Arabidopsis thaliana*), but also applies to each of the first four sequences disclosed in Figure 1, namely *Arabidopsis thaliana*, *Lupinas albus*, *Capsicum annuum* and another synthase of *Arabidopsis thaliana*, respectively.

As a result, one of skill in the art would recognize that Applicants have fully disclosed the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ with at least six examples; having express data in *Sulfolobus acidocaldarius* in wild-type and 5 different mutants, as well as data drawn by analogy in at least three other species.

Hence, the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ in prenyl diphosphate synthases is supported by the original disclosure. Withdrawal of the objection is therefore requested.

112, 2nd Paragraph, Rejections

[21] Claims 1 and 17 have been amended to clarify the term "shorter."

[23] The term "region II" in claims 1 and 17 has been replaced with "a conserved region" for clarification. The claimed amino acid sequence is in a conserved region of the mutant prenyl diphosphate synthase.

[29a] The language "an enzymatic activity in the synthesis of prenyl diphosphate" recited in claims 2 and 18 refers to the enzymatic activity of the mutant in synthesizing prenyl diphosphate as being comparable to the enzymatic activity of the wild type in synthesizing prenyl diphosphate.

[29b] Claims 3 and 19 have been amended to recite "mutant prenyl diphosphate synthase."

112, 1st Paragraph, Rejections

[30] Submitted herewith is a status of claims and support for claim changes in accordance with 37 C.F.R. 1.173(c).

[31] Applicants traverse the rejections of claim 17-32 as containing new matter. As set forth above in [14], Applicants submit that the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ is disclosed in the original claims and specification.

[32] Claims 7 and 23 have been amended to clarify the claimed thermostability, as shown in Fig. 2 and col. 13, ll. 14-19 of the specification.

[34] Applicants traverse the assertion that the specification does not provide sufficient written description of all species of the claimed genus of mutant prenyl diphosphate synthases. Claims 1 and 17 clearly recite the structural features required by members of the claimed genus, including the claimed sequence, the claimed substitution, addition, or both of an amino acid, and the claimed synthesis of farnesyl diphosphate. Accordingly, one skilled in the art would recognize that Applicants fully possessed the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ in prenyl diphosphate synthases at the time of filing. As set forth in [14] above, Applicants have fully described the sequence ($D_1D_2X_1(X_2X_3)X_4D_3$) with at least six examples; having express data in *Sulfolobus acidocaldarius* in wild-type and 5 different mutants, as well as data drawn by analogy in at least three other species. Applicants believe this is sufficient to satisfy the written description requirement.

[35] Applicants traverse the assertion that the specification does not provide enablement for the claimed mutant synthases, the encoding DNA and RNA, the host organism, and the processes. Applicants have fully enabled the sequence $D_1D_2X_1(X_2X_3)X_4D_3$ since they have provided a clear working example within the *Sulfolobus acidocaldarius* species and have additionally provided the sequence information for practicing the invention in at least four other sequences and at least three other species. One of skill in the art would, as a result, be able to practice the invention without undue experimentation using the information and methods provided by Applicants to provide the claimed mutant synthases, the encoding DNA and RNA, the host organism, and the processes.

Double Patenting Rejections

[36], [37] Applicants will attend to the provisional double patenting rejections at such time as claims in the present application are allowed.

CONCLUSION

The claims are believed to be allowable.

The Examiner is invited to contact the undersigned to discuss any issues related to this application.

The Office is authorized to charge any fees or credit any overpayment regarding this application to Kenyon & Kenyon Deposit Account No. 11-0600.

Respectfully submitted,

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